CLAIMS

What is claimed is:

1. An isolated nucleic acid sequence of SEQ ID NO: 2.

2. The isolated nucleic acid sequence of claim 1, wherein the nucleic acid sequence is DNA.

3. An isolated amino acid sequence of SEQ ID NO: 4.

4. A nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:4.

5. A replicative cloning vector comprising the nucleic acid sequence of claim 1 and a replicon operative in an isolated host cell.

6. An isolated host cell transformed with the replicative cloning vector of claim 5.

7. An expression vector comprising the nucleic acid sequence of claim 1 operably linked to a transcription regulatory region.

8. An isolated host cell transformed with the expression vector of claim 7.

9. A method for testing a substance as a therapeutic agent for bone modulation in a host comprising administering the nucleic acid of claim 1 to the host, and assessing whether bone modulation occurs.

10. The method of claim 9, wherein the host is a cell or an animal.

11. The method of claim 10, wherein the animal is a human, a rodent or a bird.

12. A method of identifying a molecule involved in bone modulation comprising identifying a molecule that binds to, or that inhibits binding of a molecule to, HBM.

13. The method of claim 12, wherein said molecule is a protein.

14. A method for identifying a protein involved in bone modulation comprising identifying a protein that has an expression level that is different in a first host comprising the Zmax1 gene when compared to a second host comprising the HBM gene.

15. The method of claim 14, wherein the host is a cell or an animal.

16. A method of identifying a candidate protein involved in bone modulation comprising

identifying a protein in a first individual having the high bone mass phenotype;

identifying a protein in a second individual not having the high bone mass phenotype;

comparing the protein of the first individual to the protein of the second individual, wherein (i) the protein that is present in the first individual but not the second individual is the candidate protein or (ii) the protein that is present in a higher amount in the first individual than in the second individual is the candidate protein or (iii) the protein that is present in a lower amount in the first individual than in the second individual is the candidate protein.

17. The method of claim 16, further comprising producing an antibody to the candidate protein.

18. A method of identifying a candidate protein involved in bone modulation comprising

identifying a protein in a first individual having the high bone mass phenotype;

identifying a protein in a second individual not having the high bone mass phenotype;

comparing the protein of the first individual to the protein of the second individual, wherein (i) the protein that is present in the second individual but not the first individual is the candidate protein or (ii) the protein that is present in a higher amount in the second individual than in the first individual is the candidate protein or (iii) the protein that is present in a lower amount in the second individual than in the first individual is the candidate protein.

19. The method of claim 18, further comprising producing an antibody to the candidate protein.

20. A method of testing for HBM activity comprising immobilizing an HBM protein, binding a protein to the HBM protein, and measuring the extent of binding.

21. The method of claim 20, wherein the protein is ApoE.

22. A method for identification of a candidate molecule involved in bone modulation comprising

identifying a molecule that binds to, or that inhibits binding of a molecule to, the nucleic acid sequence of SEQ ID NO: 1;

identifying a molecule that binds to, or that inhibits binding of a molecule to, the nucleic acid sequence of SEQ ID NO: 2; and

comparing the extent of binding, or the extent of inhibition of binding, of the molecule to each nucleic acid sequence, wherein the molecule that binds, or inhibits binding, more or less to the nucleic acid sequence of SEQ ID NO: 2 or the nucleic acid sequence of SEQ ID NO: 1 is the candidate molecule.

23. The method of claim 22, wherein the candidate molecule is a protein or an mRNA.

24. A method of pharmaceutical development for treatment of bone development disorders comprising identifying a molecule that binds to the amino acid sequence of SEQ ID NO: 4.

25. The method of claim 24, wherein the molecule inhibits or enhances the function of the amino acid.

26. A method of pharmaceutical development for treatment of bone development disorders comprising

constructing a first host that contains the Zmax1 gene or protein;

constructing a second host that contains the HBM gene or protein;

analyzing a difference between the first host and the second host;

identifying a molecule that, when added to the first host, causes the first host to exhibit a characteristic feature of the second host.

27. The method of claim 26, wherein the host is a cell-free extract, a cell or an animal.

28. The method of claim 26, wherein the difference is a surrogate marker.

29. A method for treating a bone development disorder in an animal comprising transferring the nucleic acid sequence of claim 1 into a somatic cell of an animal suffering from a bone development disorder.

30. The method of claim 29, wherein the animal is a human or a bird.

31. A method for treating a bone development disorder in an animal comprising transferring the nucleic acid sequence of claim 1 into a germ-line cell of an animal suffering from a bone development disorder.

32. The method of claim 31, wherein the animal is a human or a bird.

33. A method of altering bone development in a host comprising administering the amino acid sequence of claim 3 to a somatic cell of a host suffering from a bone development disorder.

34. The method of claim 33, wherein the host is a human or a bird.

35. A method of altering bone development in a host comprising administering the amino acid sequence of claim 3 to a germ-line cell in a host suffering from a bone development disorder.

36. The method of claim 35, wherein the animal is a human or a bird.

37. A method of treating osteoporosis comprising administering the amino acid sequence of claim 3 to a patient in need thereof.

38. The method of claim 37, wherein the patient is a human or a bird.

39. A method of treating osteoporosis comprising administering the extracellular domain of the amino acid sequence of claim 3 to a patient in need thereof.

40. The method of claim 39, wherein the patient is a human or a bird.

41. A method of treating osteoporosis comprising administering the intracellular domain of the amino acid sequence of claim 3 to a patient in need thereof.

42. The method of claim 41, wherein the patient is a human or a bird.

43. A method for treating bone development disorders comprising administering a molecule that binds to the nucleic acid sequence of claim 1 to a patient in need thereof.

44. The method of claim 43, wherein the patient is a human or a bird.

45. A method for treating bone development disorders comprising administering an antibody to a patient in need thereof, wherein the antibody is to the amino acid sequence of claim 3.

46. A method for diagnostic screening for a genetic predisposition to a bone development disorder comprising screening a sample from a patient with a nucleotide sequence derived from the genomic or cDNA nucleic acid sequence of HBM.

47. A diagnostic assay for bone development disorders comprising an antibody to the HBM protein.

48. A method for identifying a genetic predisposition to bone development disorders comprising performing a haplotype analysis using the nucleic acid sequence of claim 1.

49. A method of expressing the HBM protein in bone tissue comprising constructing an expression vector comprising a promoter that directs expression in bone tissue operably linked to the nucleic acid sequence of claim 1.

50. The method of claim 49, wherein the promoter that directs expression in bone is an osteocalcin promoter, a bone sialoprotein promoter or an AML-3 promoter.

51. A bacterial artificial chromosome having the nucleic acid sequence of SEQ ID NO: 5, 6, 7, 8, 9, 10 or 11.

52. A method for amplifying a nucleotide polymorphism in the Zmax1 gene comprising using the bacterial artificial chromosome of claim 51.

53. A method for amplifying a nucleotide polymorphism in the HBM gene comprising using the bacterial artificial chromosome of claim 51.

54. A method for identifying a regulatory element of a HBM gene comprising using the bacterial artificial chromosome of claim 1 or claim 51.

55. An isolated nucleic acid sequence comprising at least 15 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO: 2, wherein one of the at least 15 contiguous nucleotides is thymine at position 582.

56. The isolated nucleic acid sequence of claim 55 that is DNA.

57. The isolated nucleic acid sequence of claim 55 that is RNA.

58. A replicative cloning vector comprising the nucleic acid sequence of claim 55 and a replicon operative in a host cell.

59. An isolated host cell transformed with the replicative cloning vector of claim 58.

60. An expression vector comprising the nucleic acid sequence of claim 55 operably linked to a transcription regulatory region.

61. An isolated host cell transformed with the expression vector of claim 60.

62. An isolated nucleic acid sequence comprising at least 15 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO: 2, wherein one of the at least 15 contiguous nucleotides is thymine at position 582, and which encodes for an amino acid sequence including a valine corresponding to valine at position 171 of SEQ ID NO: 4.

63. The nucleic acid sequence of claim 62 which is DNA.

64. An isolated nucleic acid segment of at least 15 contiguous nucleotides including a polymorphic site from the nucleic acid sequence of SEQ ID NO: 2 in which G at position 582 is replaced by T, and sequences complementary thereto.

65. The isolated nucleic acid segment of claim 64, wherein said complementary sequence is the reverse complement.

66. The isolated nucleic acid segment of claim 65, wherein said reverse complementary sequence is mRNA.

67. The isolated nucleic acid segment of claim 64 that is DNA.

68. The isolated nucleic acid segment of claim 64 that is cDNA.

69. The isolated nucleic acid segment of claim 65 that is RNA.

70. An isolated nucleic acid segment of at least 15 contiguous nucleotides including a single nucleotide polymorphic site from an exon sequence selected from the group consisting of:

SEQ ID NO: 9 wherein nucleotide 69169 is replaced by A,

SEQ ID NO: 9 wherein nucleotide 27402 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 27841 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 35600 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 45619 is replaced by A,

SEQ ID NO: 9 wherein nucleotide 46018 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 46093 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 46190 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 50993 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 51124 is replaced by T,

SEQ ID NO: 9 wherein nucleotide 55461 is replaced by T,

SEQ ID NO: 9 wherein nucleotide 63645 is replaced by A,

SEQ ID NO: 9 wherein nucleotide 63646 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 24809 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 27837 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 31485 is replaced by T,

SEQ ID NO: 9 wherein nucleotide 31683 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 24808 is replaced by G,

SEQ ID NO: 8 wherein nucleotide 31340 is replaced by C,

SEQ ID NO: 8 wherein nucleotide 32538 is replaced by G,

SEQ ID NO: 8 wherein nucleotide 13224 is replaced by G,

SEQ ID NO: 8 wherein nucleotide 21119 is replaced by A,

SEQ ID NO: 8 wherein nucleotide 30497 is replaced by A,

SEQ ID NO: 9 wherein nucleotide 24811 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 68280 is replaced by A, and

sequences complementary thereto.

71. The isolated nucleic acid segment of claim 70, wherein nucleotide 21119 of said exon sequence of SEQ ID NO: 8 is replaced by A.

72. The isolated nucleic acid segment of claim 70 that is DNA.

73. The isolated nucleic acid segment of claim 70 that is RNA.

74. The isolated nucleic acid segment of claim 64 or claim 70 which is a probe or a primer.